REMARKS

I. Amendments to the Specification and Claims

The specification at page **[0025]** states that "all documents cited [herein] are, in relevant part, incorporated by reference". The specification has been amended to recite water insoluble polymers such as waxes, cellulose acetate, cellulose butyrates, cellulose propionate, mixed cellulose esters, acylated polysaccharides, polyurethanes, polyacrylate and polymethylacrylate polymers and derivatives. These amendments are believed to be supported by US 5,120,548 (column 4, lines 54-62) and WO 98/18610 (page 21, lines 20-30), both of which are incorporated by reference.[1]

Claim 1 has been amended to recite the water-insoluble polymers of claim 7, the water insoluble polymers disclosed in US 5,120,548 and WO 98/18610 as discussed above, and at paragraph **[0034]** of the specification.

Claims 5 and 10 have been amended for consistency with claim 1, and minor amendments have been made to claims 2-11 and 24 to improve readability. New claims 25-40 are directed to narrower embodiments of the present invention, and are believed to be supported by the originally filed claims, as well as the specification at paragraphs **[0033]-[0036]**. No new matter is believed to have been added. Claims 1-11 and 24-40 are active.

II. Interview with Examiners Barham and Woodward of October 2, 2007

Applicants wish to thank Examiners Barham and Woodward for discussing the outstanding rejections with Applicants' representatives on October 2, 2007. During the discussion, Applicants' representatives pointed out the deficiencies of the references cited under 35 U.S.C §103 (*see* detailed discussion, below).

In regard to the rejection under 35 U.S.C. §112, first paragraph, Applicants' representatives noted that the specification provides detailed examples which would allow the skilled artisan to practice the claimed invention, and the Office is already on record stating that the specification is enabling for cyclobenzaprine hydrochloride compositions according to the claimed invention (*see* detailed discussion, below).

[1] disclosed respectively in paragraphs **[0005]** and **[0011]** of the present specification

III. Rejection under 35 U.S.C. § 103

Applicants respectfully traverse the rejection of the claims under 35 U.S.C. §103 over *Patel* (US 2003/0215496) or *Meadows* (US 2003/0099711).

A. *Patel*

Claim 1 recites a dosage form comprising extended release beads, wherein the extended release beads comprise cyclobenzaprine (or pharmaceutically acceptable salts or derivatives thereof) coated with a water insoluble polymer membrane (selected from specific water insoluble polymers) and having a drug release profile such that after 2 hours, no more than about 40% of the cyclobenzaprine is released; after 4 hours no more than about 40-65% of the cyclobenzaprine is released; and after 8 hours, from about 60-85%% of the cyclobenzaprine is released.

Patel discloses "solid pharmaceutical compositions" which can include any of the pharmaceutically active ingredients disclosed in paragraphs **[0035]-[0039]** and **[0041]-[0045]**, any of the different surfactants disclosed in paragraphs **[0051]-[0114]**), any of the solubilizers disclosed in paragraphs **[0124]-[0130]**, any of the enzyme inhibitors disclosed in paragraphs **[0135]-[0139]**, and any of the other additives disclosed in paragraphs **[0144]-[0165]**. *Patel* also discloses drug release profiles ranging from "immediate release" to "extended release" or "delayed release" (i.e., paragraphs **[0169]**). In other words, *Patel* describes a huge number of different pharmaceutically active ingredients and excipients which could be combined in a vast number of different combinations. However, *Patel* does not provide any guidance for selecting cyclobenzaprine from among the many pharmaceutically active ingredients disclosed, *Patel* does not provide any specific direction that the pharmaceutically active ingredient be coated with a water insoluble polymer in preference to the many other options presented therein, nor does *Patel* suggest the specific drug release profile of the claimed invention, in preference to other quite different release profiles (*i.e.*, immediate release).

Thus, Applicants submit that the generic disclosure of *Patel* is so broad and all-encompassing that it provides little useful direction leading the skilled artisan to the compositions of the claimed invention. *See*, e.g. *in re Baird*, 29 USPQ2d 1550 (Fed. Cir.

1994) at 1552 ("A disclosure of millions of compounds does not render obvious a claim to three compounds").

The examples of *Patel* also fail to direct the skilled artisan to the claimed pharmaceutical dosage form having the claimed release profile. None of the examples disclose cyclobenzaprine-containing compositions, and the release profiles for the exemplary compositions are quite different from that of the claimed dosage forms. For example, whereas the claimed composition releases "no more than about 40%" of cyclobenzaprine after 2 hours, and "about 60-85%" after 8 hours, the compositions of Examples 2, 3, and 6 of *Patel* release about 60-70% of the drug at 2 hours (*see* Figures 1 & 2A) or exhibit a "plateau" after releasing about 10-20% of the drug at 2 hours (*see* Figure 2B); and the compositions of Examples 7 and 8 release 70-100% of the drug at only 1 hour (*see* Figure 3). Thus, the drug dissolution profiles expressly disclosed in *Patel* are substantially different from the claimed drug release profiles.

Moreover, Applicants note that the coated compositions exemplified in *Patel* exhibit drug release rates which are more rapid than even the uncoated "pure bulk drug" (*see* Figures 1, 2A, and 2B), and *Patel* further states that this drug release profile is "superior"[2] to that of the pure bulk drug. In other words, the compositions exemplified in *Patel* are immediate release compositions which *accelerate* drug release (relative to the pure drug itself), whereas in the claimed invention, drug release is *slowed* by addition of the extended release coating (*e.g.*, *see* Figure 4 in the present specification which shows reduced cyclobenzaprine release rates as coating weights increase). Thus, *Patel* teaches away from the claimed invention by directing the skilled artisan to immediate release compositions with drug release rates which are higher than that of uncoated "pure bulk drug".

Accordingly, for the reasons presented above, *Patel* not only fails to suggest the claimed invention, *Patel* actually directs the skilled artisan to compositions which are substantially different from those of the claimed invention.

[2] *Patel*, paragraph **[0280]**

B. *Meadows*

Meadows describes oral pharmaceutical preparations in which the drug is complexed with small particles of an ion-exchange resin (paragraph **[0009]**). *Meadows* discloses numerous different possible drugs (i.e., paragraphs **[0029-0030]**), and further teaches that the drug-resin complexes only "[o]ptionally ... may have at least one coating" (emphasis added)[3]. Thus, *Meadows* teaches that the drug containing particles need not be coated.

As in *Patel*, *Meadows* does not disclose any examples of cyclobenzaprine containing compositions, and the release profiles disclosed by *Meadows* are quite different from those of the claimed invention. For example, all of the compositions of Figure 4 of *Meadows* show drug release values exceeding 40% at 2 hours, as do Formulations 7-9 in Figure 5.

Furthermore, the only disclosure in *Meadows* of drug release at times greater than 2 hours is provided by Figure 6, in which all of the compositions exhibit a drug release "plateau" after 2 hours – at 2 to 8 hours, very little additional drug release occurs, with less than 60% total drug release after 8 hours. In contrast, the claimed dosage forms release "no more than about 40%" after 2 hours and "60-85%" of cyclobenzaprine is released after 8 hours. Thus, the drug release profiles of the compositions of *Meadows* are substantially different from the claimed drug release profiles.

Thus, like *Patel*, the disclosure of *Meadows* is too broad to reasonably suggest the claimed dosage form or provide sufficient guidance to modify the compositions disclosed therein to provide the claimed composition. Furthermore, the composition exemplified in *Meadows* have drug release profiles which are substantially different from the claimed dosage forms, and therefore would reasonably direct the skilled artisan to compositions quite different from the claimed dosage forms.

Accordingly, for these reasons, *Meadows* cannot reasonably suggest the claimed invention.

[3] *Meadows* at paragraph **[0021]**

IV. Rejection under 35 U.S.C. §112, First Paragraph

The Examiner states that the specification "does not reasonably provide enablement for any and all water insoluble polymers, plasticizers and water soluble polymers." Applicants respectfully disagree.

First, Applicants note that the Office has already taken the position that claims nearly identical to the pending claims *are* "enabled for use with cyclobenzaprine hydrochloride".[4] Thus, Applicants respectfully submit that the Office is estopped from rejecting the claims on this basis in view of the Office's prior, directly contradictory position.

Furthermore, the amended claims now recite dosage forms with an extended release coating comprising specific water insoluble polymers, and therefore are not directed to compositions comprising "any and all water insoluble polymers".

Moreover, the specification provides a substantial and detailed description of compositions and methods for preparing the pharmaceutical dosage forms of the claimed invention, as well as a number of different specific examples of cyclobenzaprine-containing pharmaceutical dosage forms according to the claimed invention. For instance, Example 3 teaches how to prepare polymer-coated cyclobenzaprine beads of the present invention, and how the release profile of the beads can be modified by adjusting the thickness of the polymer coating (*see* Figure 4 of the present specification). Applicants respectfully submit that the skilled artisan, presented with such an extensive description and examples would have sufficient guidance to prepare dosage forms according to the claimed invention, comprising a cyclobenzaprine-containing core particle coated with an extended release coating comprising the recited water insoluble polymers.

Accordingly, for the reasons stated above, Applicants respectfully submit that the claimed invention is enabled by the disclosure of the present specification.

[4] Office Action of January 13, 2006, at page 7; Office Action of July 10, 2006, at page 10

V. Conclusion

For the reasons stated above, Applicants respectfully submit that the claims are now in condition for allowance, early notice of which is respectfully requested. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney – as suggested during the interview with Applicants' representative on October 2, 2007 – to discuss any remaining issues and to expedite the eventual allowance of the claims.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. 1.136(a)(3).

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